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SUBSTITUTE SPECIFICATION

SPECIFICATION

TITLE

"CARDIAC PACEMAKER WITH ADJUSTABLE STIMULATION INTERVAL"

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention is directed to a cardiac pacemaker, and in particular to a cardiac pacemaker wherein the stimulation interval between stimulation pulses is adjustable.

Description of the Prior Art

A generally known cardiac pacemaker is the so-called QT-or stimulus-T pacemaker such as is described for example in United States Patent No. 4,228,803. Such a pacemaker has means with which the median stimulation frequency can be adapted to changes in physical and psychic stress.

To this end a circuit is provided which evaluates the ECG signal derived intracardially, detecting the beginning or the maximum of the T wave. Since the time interval between stimulation and the start of the T wave, the so-called stim-T interval shortens with increasing stress, the circuit delivers a physiological measuring parameter with which the stimulation frequency can be adapted to changing stresses.

The principle disadvantage of a frequency control system of this kind is due to the fact that the stim-T interval does not shorten only with an increase in stress, but shortens to a considerably greater degree through the rise of the stimulation frequency itself. Frequency control of this type

correspondingly requires special measures in order to avoid positive feedback.

A further disadvantage of this system of frequency control is the fact that the measured stim-T intervals are dependent on hormonal secretions, i.e., they respond to hormones secreted by the adrenal cortex and transported via the blood circulation.

In principle, in the regulation of the stimulation frequency in cardiac pacemakers it is an essential goal to adapt the stimulation frequency not only to rising physical stresses, but also to take into account the individual myocardial capacity of the patient. This means that the stimulation frequency is increased with rising stress only as long as a rise in the heart time volume (HTV) is achieved. This is intended to prevent the myocardium from being overloaded and damaged by too high a stimulation frequency ("overpacing").

An attempt has been made to achieve this control by measuring the beat volume BV or an HTV-dependent measuring parameter, such as for example the central venous oxygenation (s02).

From PCT Application WO 89/06990 a method is known for hemodynamic optimization of the stimulation frequency, which uses the measurement of the central venous oxygenation s02, dependent on the heart time volume, in combination with a modulation of the stimulation frequency ΔHR over phases of two to four minutes. Optimization of the heart time volume is sought in that the frequency-dependent gradient of the

oxygenation AsO2/ΔHR is kept within a predetermined range, which is a physiologically optimum range analogous to the gradient of the heart time volume HTV/ΔHR.

This method depends on the stability and the accuracy of the s02 sensor catheter, which in practice have not proved to be sufficient, and the method has the disadvantage that on account of the necessary long change periods it is not possible in the necessary time of a few minutes to differentiate whether the measured s02 change is caused by the frequency change or by other influencing variables.

European Application 0 551 355 describes a method for modulating individual stimulation intervals in which the impedance measurement is used to detect the beat volume, in order to avoid the use of a sensor catheter to determine the heart time volume. Through the deliberate modulation of individual stimulation intervals ΔSI and the phase- specific demodulation of the impedance change ΔZ, an attempt was made to suppress the influence of non- function-specific and thus disturbing parameter changes, and in addition the signal was calibrated with the aid of maximum modulation.

This method has the disadvantage that the principle of modulating individual stimulation intervals here is only used as a filtering and calibration method, i.e. as an interim step to determine the beat volume and thus the heart time volume (HTV). Optimization of the frequency control is then also sought by the optimization of the gradient ΔHTV/ΔHR on the basis of an optimum hemodynamic characteristic curve. The determination of the beat

volume, despite an improvement in the signal-to-noise-ratio as a result of the individual pulse modulation, has in practice still proved too inaccurate to be able to carry out reliable hemodynamic optimization. This means that optimization of the stimulation by controlling the heart time volume has in practice been problematic, since either the specific sensor catheters for measuring the beat volume or the HTV-dependent measuring parameters still have no adequate long-term stability, or measurements of the beat volume using standard catheters via the impedance are not sufficiently reliable. Moreover the evaluation becomes very complex since the mechanical transmission functions also detected and which falsify the measuring result must also be taken into account.

SUMMARY OF THE INVENTION

An object of the invention is to provide a cardiac pacemaker which renders possible quick and accurate regulation of the stimulation frequency or respectively of the duration of the stimulation interval, and overloading by too high a stimulation frequency is avoided.

The above object is achieved in accordance with the invention in a cardiac pacemaker having a pulse generator which emits stimulation pulses respectively separated by stimulation pulses respectively separated by stimulation intervals, each having a stimulation interval duration, and which collectively have an average duration, and a lead connected to the pulse generator which is adapted to deliver the stimulation pulses to a heart as well as to receive a signal containing action potential information from the heart,

a modulation device connected to the pulse generator which alternatingly shortens and lengthens the stimulation interval without change the average duration, thereby cause the pulse generator to emit modulated stimulation pulses, a detector connected to the lead to detect the signal received from the heart after each modulated stimulation pulse, and an evaluation unit connected to the detector for analyzing the detector output therefrom. The evaluation unit determines the electric restitution of the heart at the average stimulation interval duration by measuring the duration of the action potential in the detector output. The evaluation unit selects a measuring variable associated with the action potential duration and identifies changes in the measuring variable caused by modulation of the stimulation intervals, relative to the average duration of the stimulation intervals, and compares the relationship between the measuring variable and the average duration to at least one predetermined value. Dependent on the result of this comparison, the average duration of the stimulation interval is controlled.

The cardiac pacemaker according to the invention which has an individually optimized regulation of the duration of the stimulation interval, avoids the necessity of determining a BV- or HTV-dependent measuring parameter and makes possible, through evaluation of the electric restitution or of the gradient of the electric restitution with the aid of the standard detection of the endocardiac ECG, a regulation of the stimulation frequency or of the duration of the stimulation interval by means of a function parameter of the heart, which directly reproduces the stress state of the

patient, changes in the capacity of the myocardium and acute worsening of myocardial performance being taken into account in the frequency adaptation. Here the modulation of individual stimulation intervals is carried out in such a way that the average adjusted interval duration does not change.

The modulation of the stimulation intervals by a positive value and a negative value is carried out continuously as well as at an interval of a number of pulses with periodic repetition.

It was found that the electric restitution curve which is determined by measuring the duration of action potential, is equivalent to that which is defined by measuring the QT or the stim-T interval of the electrocardiogram.

Furthermore it has been shown that the analysis of the load- and frequency-dependent modulation of the stim-T interval is sufficiently reliable if the modulation of an individual stimulation interval gives the20inequations ESI (Extrasystolic Interval) <600ms with $\Delta ESI/BCL \geq 10\%$ (BCL = basic cycle length).

As the evaluation variable of the electric restitution, (advantageously a dimensionless variable), the gradient (ERG) or the relative change in the electric restitution can be used, for example, in order to achieve load-dependent control. This is possible because this gradient coincides with the rise in the physical load, while it rises with increasing stimulation frequency. Moreover it was also found that the change reaction is based mainly on a change in the time constants of the exponential restitution function and this

time constant reacts substantially more quickly and more strongly to changes in the load and the frequency than does the stim-T interval in a control system according to the prior art.

Furthermore the control system according to the invention can be used well in cases of acute ischemia since the electric restitution reflects the myocardial conditions. The time constant of the exponential electric restitution, and also the gradient of same, rises with the ischemia. According to the invention this causes a reduction in the stimulation frequency.

The control system according to the invention using a single pulse modulation and detection of the electric restitution causes a quick and accurate regulation of the stimulation frequency, since the electric restitution is controlled mainly by a quick reaction mechanism controlled by neurons.

DESCRIPTION OF THE DRAWINGS

Fig. 1 shows the characteristic course of an electric restitution curve of a normal healthy myocardium in a resting phase and in a load phase.

Fig. 2 shows characteristic curves for the electric restitution gradient as a function of the stimulation frequency in the rest phase and the load phase.

Fig. 3 shows characteristic curves of the gradient of the electric restitution dependent on the stimulation frequency given the occurrence of ischemia.

Fig. 4 is a block diagram of an embodiment of a cardiac pacemaker constructed and operating in accordance with the principles of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The dependence of the duration of the action potential 5 AP of the myocardium as a function parameter of the duration of the diastole t_d is designated as electric restitution. If this is spontaneously changed during a single heart cycle, for example through an extrasystole, then the action potential or its duration changes. The duration of the action potential is defined by the interval between the beginning of the stimulation and the time at which the action potential has sunk by 90%, and it decreases if the time interval between two successive stimulation pulses becomes smaller. Here a distinction is to be made between the APD change after an extrasystolic stimulation interval and the APD change after a change in the median or basic heart frequency (HR = 1 BCL) according to prior art.

This alteration behavior after an extrasystolic stimulation interval can be described by a double exponential function which is referred to as the electric restitution curve ER.

The electric restitution curve (ERC) is thus defined as 25 a function of the action potential duration APD of the cycle length of a previous extrasystolic stimulation pulse interval ESI, i.e. of an individual stimulation pulse interval which is changed from the basic cycle length (BCL), i.e. the

median stimulation interval duration by ±ΔESI, and which corresponds to the diastole.

The function can be described as

$$ER\ APD(ESI) = APD_{p1}(1-A1*\exp(\sim t_d/T1)-A2*\exp(-t_d/T2)).$$

Herein, APD_{p1} is the plateau value, A1 and T1 are the amplitude and time constant of the quick phase of the restitution and A2 and T2 are the amplitude and time constant of the slow phase of the restitution.

The distinction in the approximate equation between a slow and a quick portion in the exponential rise of the restitution curve takes into account the fact that functions of the myocardium or of the myocardial cell are determined at the cell membrane like the ion exchange, i.e. both through quick autonomous regulating processes in the cell and the surrounding tissue and also through regulating processes which affect the whole heart-cardiovascular system and are controlled by the sympathetic nervous system and the corresponding gland functions.

As a measuring parameter to determine the electric restitution curve, as indicated above, in principle the action potential duration APD is determined which can be measured by special electrodes. Tests have shown however that in measuring the ECG also the so-called QT interval, i.e. the duration of the interval between the Q peak and the end of the T wave of the intracardiac ECG has the same restitution characteristic as the APD. When stimulating the ventricle with a cardiac pacemaker 25 it is more expedient to measure, instead of the QT interval as the measuring interval,

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the stim-T interval STI, i.e. the interval between stimulation pulse and T wave.

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Fig. 1 shows, as the electrical restitution 30 curve (continuous line), the course of the action potential duration APD in dependence on the length of individual extrasystolic intervals of a normal healthy myocardium for the rest phase and for a load phase. Here in both phases respectively the optimum adapted stimulation frequency HRo or the optimum basic cycle length BCLo =1/HRo (i.e. the median duration of the stimulation interval) was changed in individual extrasystolic stimulation intervals ESI and then the corresponding change in the action potential duration APD was measured. The restitution curves thus produced correspond to the exponential functions described by the above equation. The optimum basic cycle length BCLo for rest (90 ms) and for a load (500 ms) are represented by the broken arrows, i.e. the respective basic cycle length or median interval duration was altered by ±ΔESI to form extrasystolic intervals, and respectively as the reaction the action potential duration or the QT- or stim-T interval was measured as the measuring parameter. Here mean durations of the stimulation interval were alternately so shortened and prolonged by positive and negative ΔESI values that the adjusted average interval duration remains the same. Preferably the ±ΔESI remains the same during a change, i.e. the interval duration is shortened and prolonged by the same value. The change can be repeated periodically at an interval of a number of pulses, however it can also be

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carried out continuously, i.e. each stimulation pulse is alternately shortened or prolonged.

The broken lines in Fig. 1 represent the curves of the QT or stim-T intervals of an ECG with continuous alteration of the basic cycle length, or respectively with continuous modulation, which is used for example in a QT pacemaker according to prior art. As can be recognized, these characteristic curves are clearly different from the electric restitution curves with a differing load, and with increasing load, in addition to a reduction of the plateau value of the respective curve with a corresponding displacement to the left also a steeper rise in the curve was measured.

The restitution curve can now be used for physiological control of the stimulation frequency HR, it being essential, as mentioned, that both the plateau value APD_{p1} and the time constants T1 and T2 are dependent on the pulse frequency HR and the level of myocardial efficiency. The stimulation frequency should therefore be so adjusted that the stimulation interval lies in the region of the plateau value APD_{p1} with any load.

In order to be able to use a simpler variable for the 10 regulation, advantageously not directly the region around the plateau value itself is selected but the gradient of the restitution curve. The gradient of the restitution curve in the respective optimum operating point, which is given by the optimum basic cycle length BCLo arises in that the extrasystolic interval ESI is altered as a percentage (ΔESI/BOL) by a defined positive +ΔESI and/or negative value -ΔESI and the resulting change in the action potential

duration +ΔAPD or -ΔAPD, shown by arrows 20 in Fig. 1, is measured. If this gradient of the electric restitution ERG = +ΔAPD/+ΔESI or ERG = -ΔAPD/-ΔESI is applied as a function of the stimulation frequency HR for the rest phase and a load phase, the course represented in Fig. 2 arises.

Fig. 2 shows that the exponential rise of the gradient of the electric restitution ERG as a function of a rising stimulation frequency HR with rising load is displaced to the right. It can be recognized that in the respective optimum heart frequency, the associated ERGo values, which correspond to the plateau values APD_{p1} in Fig. 1, have approximately the same level, however the values can also be different. These values can be selected in a frequency control system as set values of the gradient of the electric restitution ERG, a region around the set value ERG being given in Fig. 2 as a range for an optimum stimulation frequency HR, which is delimited by the threshold values ERG1 and ERG2.

It is also conceivable that the gradient of the electric restitution ERG is determined from the difference between the positive and negative changes in the action potential duration in relation to the positive and negative interval changes, namely with ERG[(+ΔAPD)-(-ΔAPD)]/{(+ΔESI)-(-ΔESI)].

On the basis of Figs. 1 and 2 it can be recognized that the electric restitution function or its gradient ERG offers the precondition for regulating the stimulation frequency since the gradient of the electric restitution ERG reacts with an increase in the stimulation frequency conversely to the rise in the physical stress, and has within a physiologically fixed defined region an

optimum value ERGo for each stress situation. From the ERG characteristic curve according to Fig. 2 it can be recognized that in the frequency control too high a stimulation frequency (overpacing) is avoided in principle.

However it is also apparent that a possible acute worsening in myocardial performance in patients can occur and can be taken into account in the adaptation of the frequency. In Fig. 3 is represented the gradient of the electric restitution via the stimulation frequency for a case in which a worsening of the myocardial performance occurs through ischemia. Fig. 3 shows that the lengthening of the stim-T interval on the occurrence of an ischemia displaces the ERG curve to the left in a case of stress, i.e. the gradient of the electric restitution reacts on a drop in the myocardial capacity as in a drop in physical stress. As a result of this, the optimum stimulation frequency PRo is reduced and thus the pre-eminent requirement is met that the ERG-dependent frequency control system prevents overpacing in a myocardium which is deteriorating pathologically.

In another example, instead of the gradient, the relative change in the electric restitution can be used by forming the quotient ΔAPD/ΔESI, in each case also the median values being able to be determined over a plurality of change cycles.

In Fig. 4 is represented an embodiment of a cardiac 10 pacemaker, with which frequency control is used in dependence on the gradients of the electric restitution function ERG.

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The functional blocks required for controlling frequency or the stimulation interval in dependence on the ERG are represented in the bordered area. As other functional blocks, which form part of the standard equipment of a normal QT pacemaker, a stimulation electrode 1 and a stimulation pulse generator supplying the stimulation electrode 1 are provided. Furthermore an ECG amplifier 2 is connected on the one hand to the stimulation electrode 1 and on the other hand to a detection stage for detecting the stim-T interval as a measuring variable. Moreover such a system contains a microprocessor, which can be programmed via a telemetry 25 stage 12, with a process control 11.

The functional blocks of the frequency control system are an HRmax/HRmin memory 7 to store the limit values of the stimulation frequency, a control stage 8 connected to the memory, to which stage a control variable ΔERG is supplied, a stimulation interval modulator 9 to fix and modulate the stimulation interval and which is connected to the stimulation pulse generator 10. Furthermore a calculation stage 4 is provided which receives a signal from the detection stage 3 and from the modulator 9, and a stage 5 to form the average value, a set value memory 6 and a set/actual value comparator 13.

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The functioning of the cardiac pacemaker is as follows. 5 The stimulation pulse generator 10 supplies a stimulation pulse to the stimulation electrode and the ECG amplifier amplifies the intracardial ECG signal derived via the stimulation electrode 1. From this amplified signal, the

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detection stage 3 analyses the interval duration STI between the stimulation pulse and the T wave which corresponds to the QT interval or the action potential duration. In the calculation stage 4, the gradient of the electric restitution ERG is calculated, however others of the above-mentioned variables can also be used. To this end first of all, triggered by the modulator 9, the change ±ΔSTI is calculated, with the stim-T interval value supplied by the detection stage, which change has been caused by the change ΔESI in the stimulation interval, and then the quotient ERG = ΔSTI/ΔESI is determined. In the median value stage 5, the median value ERGm of the ERG values is calculated over a plurality of change cycles. With the arrow from the exit of the median value stage 5 to the set value memory 6 is indicated that the ERGm value, which in the body's rest state is measured at a median stimulation frequency of roughly 90/min, is stored as the set value.

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In the set Value/actual Value Comparator 13, the difference between the median value of the gradient of the electric restitution ERGm and the set value ERGs is formed, and is given as the difference value ΔERG to the control stage 8, the latter being used to adjust the median stimulation frequency HR_0. This is calculated for example with the aid of the following functions:

$HR_o = HR_{min} + k^*\Delta ERG$,

wherein HR is so regulated that HR is < HRmax. Here HRmin and HRmax are minimum or maximum frequencies which can be predetermined by

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external programming and stored in the memory 7, and k is a proportionality factor. HRmin is generally predetermined by the optimum median stimulation frequency HRo in the rest state. The basic frequency HRo thus determined is supplied to the modulation stage 9, in which the basic cycle length BOL = 1/HRo is modulated periodically with an interval change ±ΔESI and the resulting stimulation interval ESI = BCLo + ΔESI is formed. In the following stimulation pulse generator 10, the stimulation pulse is then output in dependence on the ESI value. The regulation is repeated until the value ΔERG is zero.

In the above-described value, as the set value for the gradient of the electric restitution ERGs, the level was selected which arises for the individual load curves according to Fig. 2 at the optimum stimulation frequency HRo, control fluctuations between the values ERG1 and ERG2 being admitted. The set value ERGs can however also be automatically adapted to longer-term fluctuations of the restitution gradient with the aid of a second measuring parameter, independent of the modulation, with which parameter it is possible to recognize the rest state of the patient. In the rest phase then the minimum stimulation rate HRmin is automatically adjusted and the set value ERGs is adapted to the restitution gradient measured at rest. In this manner, the set value is "recalibrated". The measuring parameter which is independent of the modulation can be supplied for example by a mechanical movement sensor. The set value can also be

adjusted in dependence on the frequency, for example it can be fixed during the rest state and then provided with a frequency-dependent slope.

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